THE RELATION OF LIFE STRESS TO CARDIOVASCULAR SYMPTOMS AND DISEASE

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For many years patients with structural heart disease have been distinguished as a group from those with cardiovascular complaints but without evidence of structural disease. The more frequent observation of overt emotional disturbances in the latter group has encouraged the separation. Studies of the last fifteen years, however, have demonstrated the occurrence of functional cardiovascular changes during emotional disturbances among all types of subjects, ranging from healthy persons without symptoms, through patients with cardiovascular complaints but no structural disease, to those with serious anatomic deformities. Moreover, it has been abundantly shown elsewhere in the body, such as for example the gastrointestinal^{34, 35} and nasorespiratory³³ systems, that sustained dysfunction may lead to significant structural change. Thus the earlier distinction between "functional" and "structural" has yielded to a more integrated view of all persons with cardiovascular disturbances. It is the purpose of this communication to review the observations from which this orientation arises and to indicate aids in the assessment and management of cardiovascular disorders related chiefly or in part to problems of personality adjustment.

Inferences have often been drawn from the temporal coincidence of life stress with its attendant emotional conflict and the occurrence of cardiovascular disturbance. In the studies reported here, however, these suggestive data have been reinforced by a validation procedure which

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depends upon the observation of such changes in a relatively controlled short term experimental situation.

FUNCTIONAL CARDIOVASCULAR CHANGES DURING EMOTIONAL DISTURBANCES

Heart Rate. Accelerations of the heart with emotional disturbances have been noted since antiquity¹ and are generally accepted as commonplace. The magnitude of such accelerations has recently been investigated in a series of interviews during which heart rates were recorded, usually by an electrocardiograph.² During the interviews the subjects discussed pertinent life situations and in doing so exhibited varying degrees of the emotional states associated with these stressful situations. The average heart rate during relaxation of forty-eight subjects thus studied was 80, and the average rate during maximal emotional disturbance was 99. Half of the patients showed increases of 20 or more beats per minute. Eight patients attained rates above 120 per minute and three attained rates above 130. The maximum change occurred in a girl with asthma whose heart rate varied from 81 when she was relaxed to 128 during a period of mixed humiliation and resentment (Fig. 92). Other studies have demonstrated the occurrence of cardiac slowing related to certain emotional conflicts.3,4

Heart Rhythm. An awareness of a relation between emotional disturbances and arrhythmias stems from the classic Greek period⁵ and in the last fifteen years has been attested to by an increasing number of case reports. 6, 7, 8, 9, 10 In a study of twenty patients with paroxysmal auricular fibrillation, Hanson and Rutledge noted the relevance of emotional factors to the occurrence of the arrhythmias in 70 per cent.¹¹ Stevenson, Duncan and others made a more detailed study of thirtyfive unselected patients with a variety of arrhythmias, including auricular and ventricular extrasystoles, auricular and nodal tachycardia and auricular fibrillation. They found that although other factors were sometimes operative, stressful life situations and emotional disturbances related to them were of paramount significance in the occurrence of the arrhythmias in every case.^{12, 13} Figure 89 illustrates typical variations in the frequency of paroxysmal auricular tachycardia with changing life situations. The day to day observation of this relationship was supplemented by the electrocardiographic recording of variations in the frequency of extrasystoles with emotional changes arising during the discussion of stressful life situations. 12 Figure 90 is an analysis of one such interview. The occurrence of such major arrhythmias as auricular fibrillation has also been experimentally related to emotional stresses.^{13, 14}

Cardiac Output and Exercise Tolerance. Increases in cardiac output associated with such states as anxiety and resentment have been re-

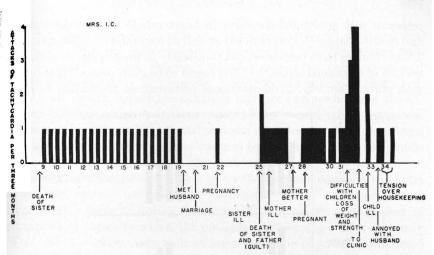


Fig. 89. Variations in frequency of paroxysmal auricular tachycardia with changes in life situations. Abscissa gives age of patient in years.

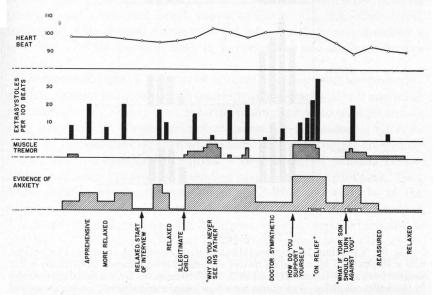


Fig. 90. Variations in frequency of ventricular extrasystoles with emotional changes. Analysis of an interview with a patient. Muscle tremor was gauged on a scale of 1 to 4 plus from the irregularities of the electrocardiograph tracing. Anxiety was similarly gauged by the voice, remarks and behavior of the patient, a 53 year old woman with arteriosclerotic heart disease. (Stevenson, I., Duncan, C. H., Ripley, H. S., Wolf, S. and Wolff, H. G., in Psychosomatic Medicine.)

peatedly observed^{15, 16, 17} as well as a shortening of circulation time.¹⁸ When there was added the stress of physical exertion, an exaggerated

response with prolonged increases in heart rate, 19, 20, 21 stroke volume and cardiac output 19, 20 were noted as well as respiratory inefficiency. 19, 22 These changes have been observed transiently in healthy subjects during periods of emotional stress, 19, 20 and found to be most marked in subjects with chronic anxiety. Mild emotional disturbances amounting to little

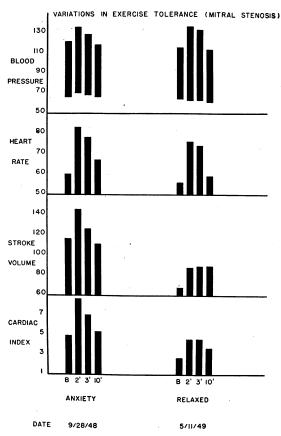


Fig. 91. Variations in exercise tolerance with emotional changes. The patient was a 45 year old woman with mitral stenosis. Measurements of cardiovascular indices were made before (B) and at 2, 3 and 10 minutes after a standard exercise in the basal condition. Symptoms were less intense and exercise easier on second day.

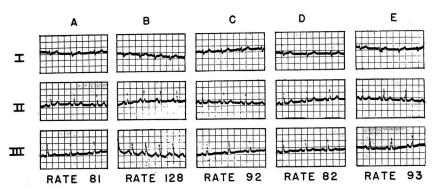
more than a preoccupation with some problem may be reflected in an increase in cardiac output.²⁰ Under certain circumstances a hypodynamic response with a fall in cardiac output has also been observed.^{4, 19}

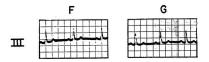
Figure 91 illustrates an example of the variability of exercise tolerance coincident with changes in the life situation and emotional state as provided by a 45 year old woman with rheumatic heart disease, mitral

stenosis and insufficiency, enlarged heart and frequent extrasystoles. When first seen she showed marked tension and hostility related to a conflict over two men. She complained of weakness, palpitations and dyspnea on exertion. Her exercise tolerance was markedly impaired. Over a six month period her situation improved somewhat and she attained insights which were accompanied by considerable relaxation. Extrasystoles almost disappeared and she was almost free of symptoms at the time of the second test of exercise tolerance, although her underlying structural heart disease was unchanged.

Blood Pressure. O'Hare²³ shortly after the clinical sphygmomanometer came into general use observed significant pressor responses among hypertensive subjects during "excitement" induced by a discussion of situations or topics to which the patients were sensitive. More recently Wolf and co-workers undertook an extensive study of variations in blood pressure and renal hemodynamics in subjects with and without hypertension.²⁴ It was found that a discussion of topics which evoked feelings of anxiety and resentment was invariably associated with a rise in blood pressure and associated renal vasoconstriction. On the other hand, feelings of dejection and defeat were not infrequently accompanied by a lowering of blood pressure both in hypertensive and nonhypertensive subjects.

Electrocardiogram. A number of authors have reported electrocardiographic changes in subjects with neurocirculatory asthenia^{25, 26} and other psychoneuroses.²⁷ Others have reported finding few or no changes among such subjects.28,29 When electrocardiograms are taken during an emotional disturbance rather than at random, abnormalities are frequently found. Mainzer and Krause studied a large group of patients before. during and after the anxiety attending major surgical operations. They found definite electrodardiographic abnormalities in two-fifths of the subjects. The changes observed included diminution in the amplitude of T waves, T wave inversions, RS-T depressions and increased amplitude of P waves. 30 Stevenson. Duncan and co-workers recorded electrocardiograms during discussions of stressful life situations with thirty-five patients both with and without structural heart disease. During the periods of maximal emotional disturbance a diminution in amplitude of 0.5 mm. or more of the T wave in one or more leads occurred in eighteen of the subjects. In eight of these the effect was of sufficient degree to change the direction of the T wave. In four patients depression of the RS-T segment was observed and in ten there was an increased amplitude of the P waves.2 Figures 92 and 93 show examples of the altered electrocardiographic patterns. During these changes the heart rate increased in most but not all instances. The wide variety of changes in different subjects showing comparable accelerations of the heart makes it unlikely that





A- RELAXED BEFORE INTERVIEW

B- ANXIOUS, CRYING WHEN TALKING OF SISTER

C-RELAXING, BUT STILL TENSE

D-RELAXED FULLY

E-AFTER EXERCISE

F-DURING A FULL INSPIRATION

G-DURING A FULL EXPIRATION

Fig. 92. Electrocardiographic changes during emotional disturbances. The patient was a 28 year old girl with asthma but without cardiovascular complaints. The changes occurred during a discussion of her psychopathic sister. They were not imitated by movements of the diaphragm which might cause rotation of the heart.

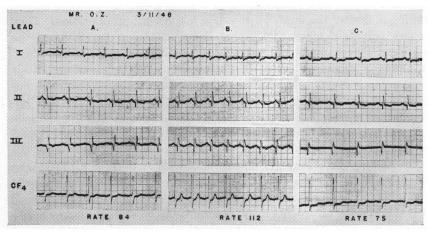


Fig. 93. Electrocardiographic changes during emotional disturbances. The patient was a 48 year old man who had a posterior myocardial infarction. Changes in the electrocardiogram occurred during discussion of his first marriage.

the changes were due solely to the tachycardia. It cannot be stated whether the changes were due to cardiac anoxemia secondary to increased work or coronary vasoconstriction or to a more direct influence of the autonomic nervous system on the electrocardiogram. The studies indicate the advisability of some knowledge of the emotional state of the subject as an aid to interpreting an electrocardiogram.

Coronary Blood Vessels. Although the occurrence of angina pectoris during emotional disturbances has been known since the celebrated case of John Hunter, the mechanism of this relationship is still obscure. Electrocardiographic changes during anginal pain related to anxiety and resentment have been reported recently.^{19, 31} In two instances reported by Wolf and Wolff, precordial pain and electrocardiographic changes occurred during changes in cardiac output.¹⁹ In one instance cardiac output was increased during resentment while coronary flow was apparently relatively inadequate. In the other, cardiac output fell during feelings of dejection and coronary blood flow was presumably decreased. Studies of other organs make it highly probable that the tone of the coronary blood vessels may be directly altered during emotional disturbances, thus producing another mechanism for angina pectoris; but there is as yet no direct evidence in support of this hypothesis.

Other Visceral Vessels. In such illnesses as migraine and central angiospastic retinopathy the occurrence of significant cranial vascular changes has been demonstrated in response to stressful life situations.³² In other organs it has been possible in such situations to observe directly changes in blood flow. Thus in the nose,³³ stomach³⁴ and colon,³⁵ the mucosa is found to become engorged and red during feelings of anxiety and resentment and paler during dejection and despair. Using the technics of Smith, renal vasoconstriction involving both afferent and efferent arterioles has been observed during anxiety and resentment^{24, 36, 37} evoked by a discussion of significant personal conflicts. Such changes in renal blood flow associated with pressor effects could also be induced in healthy subjects but occurred in greater degree among the hypertensive group.

Peripheral Blood Vessels. A relationship between the peripheral circulation and emotional changes has been inferred from the course of such conditions as Raynaud's syndrome³⁸ and documented by quantitative experimental studies of digital temperature⁴⁰ and pulse amplitude as measured by the plethysmograph.⁴¹ Graham has recently shown abrupt variations in the tone of small cutaneous blood vessels with emotional stress and has demonstrated that they are related to the occurrence of such skin disorders as urticaria and eczema.⁴² With regard to the circulation of the skeletal muscles it appears that the increased cardiac output shown to be associated with anxiety is not directed to

the kidney or other viscera, but in man as in animals,³⁹ is distributed to the skeletal muscles.

RELATION OF PERSONALITY, ATTITUDES AND EMOTIONAL STATES TO CARDIOVASCULAR PATTERNS

Such multifarious circulatory disturbances as accompany life stress are difficult to explain according to old concepts of neural imbalance and organ inferiority, but when they are viewed as integrated patterns of defense, somewhat inappropriately used, they take on more significance.

The commonest pattern encountered may be described as that of cardiovascular mobilization. This pattern attends anxiety and resentment in which there is an actual or symbolic intention of aggression or vigorous defense. The cardiovascular pattern has its biological origin in the preparation of the body for appropriate physical action.³⁹ Accordingly, there is an increase in heart rate and stroke volume, some rise in blood pressure and a fall in peripheral resistance with presumable redistribution of blood from viscera to skeletal musculature. Changes in other systems, such as respiratory hyperactivity are usually associated. The continuance of the emotional disturbance during exertion leads to an exaggerated response to effort. The subject may be aware of a wide variety of symptoms such as dyspnea, palpitations and giddiness. This syndrome is frequently described as "neurocirculatory asthenia," but this term, by suggesting a disease entity, obscures the fact that the symptoms are not fixed but fluctuate with the emotional state of the subject. When the syndrome becomes habitual, it is found, as might be expected, in subjects who are timid, passive, and dependent, and who have little conscious hostility, but much unbound anxiety which is markedly increased in any stressful situation.

A much more lethal category of cardiovascular hyperfunction includes essential hypertension. The cause of this disorder is by no means established, but there is considerable evidence that personality problems are in some way relevant to it. Associated with the mobilization pattern described above there occurs an increase rather than a decrease in peripheral resistance, and, of course, a substantial elevation of blood pressure with accompanying renal ischemia. The personality characteristics of subjects with hypertension differ sharply from those with neurocirculatory asthenia. Fifty patients out of fifty-eight carefully studied generally fitted the following description. They were nonreflective and displayed a taste for dealing with problems by action. From the standpoint of attitudes as well as circulatory physiology they were mobilized for combat, but did not engage in it against the pertinent adversary. Under an appearance which was often affable and easy going, they were tense, wary and suspicious, afraid of committing themselves. They were poised

to strike, but withheld their punch with a guilty fear of its consequences. At the same time they displayed a strong need to conform and keep peace. This, coupled with inability to throw themselves wholeheartedly into things because of fear and suspicion, made it difficult for them to believe strongly in anything or to derive real satisfaction from their accomplishments. They felt a need to show provess without exhibiting aggression and continually feared that they would not succeed in doing so.

The pattern of cardiovascular hyperactivity is closely related to the occurrence of arrhythmias. In the previously mentioned study, arrhythmias^{12, 13}were found to occur usually in patients who were serious, conscientious, hard-working, perfectionistic and compulsive. They also showed evidence of longstanding anxiety. Although sensitive to frustrations in their progress, fear of reprisal led them to repress and suppress the hostility which such frustrations aroused. In such a setting, mounting tension was associated with a sustained state of cardiovascular mobilization. The irritability of the heart was thereby increased until at the end of some hours or days an arrhythmia ensued. Patients with structural heart disease being less able to endure such hyperactivity were found to develop arrhythmias more readily than subjects with structurally normal hearts.

Less commonly observed, but nonetheless important is the phenomenon of cardiovascular hypoactivity. Slowing of the heart, fall in cardiac output and in blood pressure have been observed in subjects who feel dejected and overwhelmed.^{4, 19} Individual subjects have been observed to react with cardiovascular hyperactivity at one time and hypoactivity at another in association with opposite attitudes and feeling states.

Mixed patterns of cardiovascular activity could also be identified. Just as an individual may be in mental conflict and feel two ways about the same thing, so may his cardiovascular apparatus be expressing divergent aims at once. Thus it has been postulated that vasodepressor syncope occurs when there is a primary cardiovascular mobilization which is abruptly inhibited by more powerful opposing drives. Blood is suddenly pooled in the extremities and syncope ensues.³

THE RELATION OF PSYCHOSOMATIC CARDIOVASCULAR PATTERNS TO STRUCTURAL DISEASE

Although functional cardiovascular disturbances related to emotional changes are of importance in any patient, they are of greatest significance when they compromise the adaptability of an already damaged heart or perhaps, by becoming unduly sustained, produce structural damage by themselves.

An already damaged heart may become exhausted by an increase in

its work accompanying the increase in stroke volume associated with anxiety, or in the presence of excessive rate⁴⁴ or arrhythmias.¹³ Congestive heart failure has been observed to be so precipitated. On the other hand, a decrease in cardiac output such as has been observed during depressive states with associated anxiety may also compromise the effective performance of the heart whose reserve is already low.^{4, 19}

The blood supply of the heart may be impaired during anxiety by increased work beyond the capacity of the coronary arteries, during depression by decreased cardiac output, and possibly also by direct changes in the caliber of the coronary vessels. These changes may lead to angina pectoris or coronary thrombosis and indirectly to heart failure.

The studies of Levy and his collaborators suggest that individuals who use the pattern of repeated and sustained tachycardia as a way of meeting threats are more susceptible to the subsequent development of structural heart disease than are those with normal heart rates.

Moreover, when unduly sustained, the emergency pattern which involves elevation of blood pressure with shunting of blood to other structures at the expense of the kidneys may ultimately be shown to result in renal ischemia and irreversible hypertension.⁴⁶

Finally, repeated or sustained vascular contractions not only in the renal vessels, but also in the cerebral and retinal as in malignant hypertension or in the digital arteries as in Raynaud's disease may lead to irreversible damage to the organs involved.

THE ASSESSMENT OF THE PSYCHOSOMATIC FACTOR

The first requirement is a detailed history with particular search for a variability in intensity of symptoms associated with events in the patient's life and his attitudes and reactions to them. Frequently it is not possible to establish these relationships on the basis of the patient's conscious awareness, but evidences of unconscious conflicts must be sought in the behavior and manner of the subject, by inconsistencies in things said and left unsaid and by "blocking" and gaps in memory.

The matter may be further clarified by observation of the patient's signs and symptoms at each interview. These can then be related to the prevailing emotional state of the patient and, if their purpose is explained, they need not focus unduly his attention on his symptoms. Occasionally, a test of function such as the exercise tolerance test⁴⁷ performed on different occasions may demonstrate to the physician and patient alike the variability of his disorder with changing emotional states. If symptoms such as flushing, blanching, tachycardia, or arrhythmias occur during discussions of disturbing topics the observation can be immediately exploited in therapy.

THERAPY

Therapy of these disorders requires attention to the person, his background, development, and present life setting. The physician may attempt by various means to uncover repressions and induce the patient to a reorientation of attitude toward people and events. This maneuver requires special technical training. The physician who is not a technical specialist, however, may accomplish a great deal by assuming a dependable and understanding attitude which allows the patient vicariously to work off his bottled-up hostilities and to expiate his guilt. It is important during this period to lend the patient sustained support and especially not to betray evidences of disapproval of his acts or statements. It is equally essential to give serious and attentive consideration to all bodily symptoms even though no explanation may be offered and no medication given for them. Much damage can be done by "brushing off" or being impatient with the patient's complaints.

An explanation of psychosomatic mechanisms as a basis for symptoms is often appropriate, but it is unwise to push such explanations if the patient does not readily accept them. Especially it is not wise to force the patient to "insight," to induce him to acknowledge a connection between his personal conflicts and his symptoms. Very often a patient will deny such a relationship and yet paradoxically will talk freely as if he was aware of the connection. This "face-saving" screen is frequently very important to the patient and there is usually little to be gained and often much to be lost by breaking it down. During discussion of events, attitudes, feelings and reactions in the day-to-day life of the subject there will usually be opportunities to help in the resolution of dilemmas and to mitigate the doubts and conflicts of indecision. Often it may be helpful to weight the balance either by direct counsel or indirectly by discussion to help the patient see the elements of a problem in healthy perspective.

Case I. An example of apparently successful therapy of this type is provided by the case of a 30 year old minor business executive who was referred to the hospital in February 1947 for consideration of surgical sympathectomy for hypertension. His complaints included lassitude, lack of energy, frequent periodic tightness in the back of the neck and shoulders, headache and a "foggy feeling" with difficulty in concentration.

In replying to questions during history taking the patient gave no evidence of being nervous or "a complainer," neither was he considered nervous by his friends. His relationship to life was apparently a bland one. He denied inner conflicts and had experienced no dramatic emotional traumas.

He was the fifth of seven children, all boys but one, born to an American family of English and Irish extraction. The father died when the patient was

3 years old, leaving the mother to support the large family and forcing them into a somewhat lower social status than they would have otherwise occupied.

The mother was highly conscientious, warm, but moralistic and ambitious for her boys. Praise was liberal for all types of achievement, especially scholastic and economic, and the atmosphere at home was friendly.

The older boys went to work early to swell the family income and it soon became clear that the patient had been singled out as the one to be sent to college and who would have the greatest opportunity for a career.

The oldest brother became wealthy and well known as the originator of a popular comic strip. He built a luxurious home for himself and became the mainstay of the family financially. He also was successful in other respects, having gained acclaim as a combat artist with the Marines.

The second brother was less successful, working as a bank teller and haber-dashery salesman. He suffered from arthritis and sinus trouble.

The third child, a sister, was apparently well and happily married.

The fourth brother was also a well paid comic-strip artist.

The patient indicated that his relations with all these brothers were cordial and constructive, apart from some slight resentment of his oldest brother's failure to provide more generously and spontaneously for the needs of himself and the family. He was closest to the brother who was next younger and who, like himself, was a minor business executive.

The youngest boy was a student at Yale who was considered to have made a more successful adjustment at college than did the patient.

The patient stated that he had always wanted to do art work but did not have enough talent. On the other hand, he excelled in sports, such as golf, and felt best while playing golf.

Physical examination revealed no abnormalities except for a blood pressure in both arms of 168/100 and in both legs of 220/130. A diagnosis of essential hypertension was made and it was decided to defer consideration of operation until an opportunity had been afforded to explore the possibility of relevant personal conflicts.

The patient was antagonistic to the thought that his symptoms might have arisen as part of a reaction to life stress and repeatedly emphasized that he was sure that there was "some physical basis" which eluded detection. He seemed reassured whenever a "physical" test procedure was carried out on him. Thus, the lowest blood pressure reading during his hospital stay (140 systolic and 85 diastolic) was recorded during the measurement of his renal blood flow by the technics of Homer Smith although the procedure had required that he be catheterized with an indwelling catheter and receive a continuous intravenous infusion over a three-hour period while lying on a hard bed. Following two twentyminute control periods during which the blood pressure remained at 140/85 and the renal plasma clearance was 675 cc. per minute, a discussion was begun in which he was asked to compare his achievements with those of his brothers and he was asked whether or not he felt that their sacrifices on his behalf were justified. He flushed slightly, appeared a little tense but was not particularly disturbed. His replies were laconic, matter-of-fact, to the effect that he had not done as well as he might have but that it was not a source of concern to him.

During this period his blood pressure rose to 160/105 and his plasma clearance fell to 535 throughout the twenty-minute clearance period. Later, when he was successfully diverted and reassured his blood pressure fell again to 135/80 but the renal plasma flow remained low.

This experiment was interpreted as indicating that there probably were relevant personal conflicts of which this patient was perhaps not altogether aware. Accordingly, he was seen in the clinic for approximately one hour at each visit twice monthly for seven months, monthly for eight months and one year later was seen monthly for three months. During these interviews he was encouraged to discuss his activities, those of the other members of his family and his attitudes toward them.

It was soon evident that many of his statements concerning his brothers were contradictory. For example, he revised his statement that he was closest to his next youngest brother saying that he disapproved of his trivial attitudes, card playing and late hours. He said he felt much closer to the one who suffered from arthritis.

He also brought out that as a child he had had a violent temper. During this period of interviews his blood pressure fell to 150/90 and remained at approximately that level. Finally, three months after he was first seen and with the aid of partial sodium amytal narcosis he stated overtly what had long been suspected, that there had been intense rivalry among the brothers for their mother's approval. He expressed feelings of guilt over the sacrifices his brothers had made to give him special opportunities and conflict over his apparent failure to justify them. He said, however, that despite these sacrifices and his college education he had felt at a disadvantage. Usually he blamed a minor head injury sustained at college. "I think that is what made the muscles in my neck tense and makes it hard to concentrate. Otherwise I would have been as successful as you, doctor." He spoke bitterly of other doctors having dropped his case after preliminary evaluation and he hoped that the writer would continue to take care of him.

During these interviews it became increasingly apparent that the patient was dissatisfied with his lot in life, depressed, tense and insecure much of the time and that he had difficulty in developing allegiances or close personal attachments. His attitude was slightly suspicious and he felt the need to "hold back" in his relations with people. As he talked over all these matters he gradually began to feel that his blood pressure was not his central problem but was a facet of a general day-to-day reaction of "holding back" and "sitting on the lid." He gradually gained confidence and ability to express himself more freely. Finally, he increased his range of social relationships and found that he was able to make much warmer associations than before, especially with girls. His blood pressure fell to and remained at 125/80 for the remaining months of observation. He had more energy and the tightness in his neck and shoulders, headache and "foggy feeling" occurred only rarely and generally at times when he was brought into close contact with his superiors at work.

Comment. It cannot be inferred that with this patient a permanent relief of hypertension has been achieved. He will probably need occasional contacts with the clinic indefinitely and he may ultimately fail to respond to this type of therapy, but at least the evidence indicates that a comprehensive view of the patient as a person, the interest and solicitude of the physician together with a "common sense" approach to the patient's day-to-day life problems and conflicts have had a salutary effect upon the course of the illness.

The most powerful therapeutic weapon, however, has been shown to be the reassurance and emotional support which stems from the attitude of the physician⁴⁸ which reflects interest, sympathy and willingness to stand by.

The managements of these problems is within the power of any intelligent physician who is interested in people and their problems and who will give sufficient time for a full psychobiological history and the exploitation of the therapeutic leads which arise from it. Psychiatric consultation may often be necessary or desirable, 48 but in general it is better for the patient to be under the care of one physician who can help him to an understanding of his problems as well as to apply appropriate therapy to the end organ when decompensation or other modifiable phenomena occur.

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